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PATREA L. PABST
ARNALL GOLDEN & GREGORY
2800 ONE ATLANTIC CENTER
1201 WEST PEACHTREET STREET
ATLANTA GA 30309-3450

| EXAMINER | |
|---|---|
| ULM, J | |
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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Paper No. 21
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Application Number: 08/765108
Filing Date: 27 March 1997
Appellant(s): Krieger et al.

Patrea L. Pabst
For Appellant

## EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 18 February 1999.

*(1) Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

*(2) Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

*(3) Status of Claims*

The statement of the status of the claims contained in the brief is correct.

*(4) Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

*(5) Summary of Invention*

The summary of invention contained in the brief is correct.

*(6) Issues*

The appellant's statement of the issues in the brief is correct.

*(7) Grouping of Claims*

Appellant's brief includes a statement that claims 11 to 15 and 19 to 22 do not stand or fall together with claims 44 to 47, claim 49 and claim 50 and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

*(8) Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

*(9) Prior Art of Record*

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Calvo et al. "Identification, Primary Structure, and Distribution of CLA-1, a Novel Member of the CD36/LIMPII Gene Family." The Journal; of Biological Chemistry, Vol. 268, No. 25 (05 September 1993), pp. 18929-18935.

*(10) Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

Claims 11 to 13, 17, 19 to 22 and 44 to 50 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is not enabling for the production of an isolated nucleic acid encoding a scavenger receptor protein lacking one of the amino acid sequences that are disclosed in SEQ ID NOs:4, 6 and 8 of the instant application for those reasons of record in section 6 of Paper Number 7. As stated therein, the text beginning on line 38 of page 38 of the instant specification states that the term " scavenger receptor BI" encompasses proteins comprising those amino acid sequences of SEQ ID NOs: 4 and 8 of the instant application "and degenerate variants thereof and their equivalents in other species of origin, especially humans, as well as functionally equivalent variants, having additions, deletions, and substitutions of either nucleotides or amino acids which do not significantly alter the functional

activity of the protein as a receptor characterized by the binding activity identified above". It is unclear from reading the instant specification what the term "the binding activity identified above" is referring to. Because there is no limitation on the nature of the "additions, deletions, and substitutions" that can be made in the disclosed amino acid sequences or the sequences of "equivalent" proteins from other organisms, the instant claims essentially encompass a nucleic acid encoding any protein which possesses the ability to bind low density lipoproteins and a plurality of methods of using that protein. The recitation of the limitation "scavenger receptor protein which selectively binds to low density lipoprotein and to modified lipoprotein having the characteristics of acetylated low density lipoprotein" is nothing more than a recitation of a biological activity which places no structural limitations on the claimed composition. Because claim 11 places no structural limitation on the claimed composition it is, in essence, a single means claim because it encompasses any composition having a recited activity whereas the instant specification only discloses those three compositions known to the inventor. As determined in *In re Hyatt*, 218 USPQ 195 (CAFC 1983) such a claim does not meet the requirements of 35 U.S.C. § 112, first paragraph, because the instant specification does not disclose any and all compositions which meet the sole functional limitation of the claims.

In so far as these claims encompass a nucleic acid which encodes a scavenger receptor protein lacking one of the two naturally occurring rodent amino acid sequences that are disclosed in the instant application or a method of using that protein, the instant specification

does not identify those amino acid residues in the amino acid sequence of SEQ ID NO:4 or 8 which are essential for the biological activity and structural integrity of a scavenger receptor protein and those residues which are either expendable or substitutable. In the absence of this information, working examples or the identification of analogous proteins for which this information is known a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 500 amino acid residues before they could even begin to rationally design a nucleic acid encoding a functional scavenger receptor protein having other than a natural amino acid sequence. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

An artisan can not alter the amino acid sequence of either of the two scavenger receptor proteins that are disclosed in the instant specification by following the guidance provided

therein and have "their performance characteristics predicted by resort to known scientific law". See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not provide an adequate written description of a nucleic acid which encodes a human scavenger receptor protein such that an artisan could make and use that nucleic acid for those reasons of record in section 4 of Paper Number 7.

This rejection is based upon the premise that, whereas a specification may be enabled for a genus of chemical compounds, it is not enabled for a specifically recited species of that genus unless it identifies that material property or combination of properties which distinguishes the claimed species from the other members of the genus to which that species belongs. In the case of an isolated nucleic acid encoding a protein "X", a generic claim which encompasses any isolated nucleic acid encoding protein "X" is enabled by nothing more than the disclosure of the amino acid sequence of protein "X" since the genetic code and nucleic acid synthesis were well known in the art at the time of the instant invention. However, a claim to "a cDNA encoding protein "X"" would require the disclosure of the nucleotide sequence of a specific cDNA before an artisan could produce the claimed cDNA **to the**

**exclusion** of all of the other nucleic acids encompassed by the generic claim "an isolated nucleic acid encoding a protein "X"". As stated in the recent decision in *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997):

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

Because the instant application does not provide a written description of those material properties which distinguish "a human scavenger receptor" from any other mammalian

scavenger receptor, a practitioner of the art can not produce the claimed nucleic acid to the exclusion of a nucleic acid encoding any other mammalian scavenger receptor. Further, the text beginning in the last paragraph on page 14 of the instant specification shows that one can not isolate a genomic DNA encoding a human scavenger receptor by employing only routine experimentation, as asserted by Appellant.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim is drawn to a method of treatment without method steps. It is drawn to a method of inhibiting the binding of a lipoprotein to a receptor protein but the claim recites no steps which would result in this inhibition, or any steps at all for that matter. This claim recites an objective but requires no activity which would lead to that objective, such as the administration or removal of a compound or agent which influences the activity to be inhibited. Appellant's traversal of this rejection as "nothing more than a rejection for lack of utility under 35 U.S.C. 101" is wholly inapplicable to this rejection.

The instant specification does not describe a single working example of a method of treatment and does not provide the guidance needed for the practice of such a method for those reasons of record in section 7 of Paper Number 7. The fact that one can identify a compound which binds to one of the proteins described in the instant invention does not enable an artisan to then routinely administered that compound in an effective manner in a clinical environment.

The vast majority of compounds with desirable properties as determine by *in vitro* assays like the binding assay of the instant invention have proven to be useless in an *in vivo* application and most of those that have proven to be useful have required a substantial inventive contribution before an effective method of administration was developed. There is no dispute that the instant specification provides a method which can be used to identify compounds which inhibit the binding of AcLDL to a protein of the instant invention but the specification lacks that inventive contribution needed to employ the compounds identified thereby in a method of treatment.

Claims 44 to 50 are rejected under 35 U.S.C. § 112, first paragraph, because they are incomplete. Each of these claims is drawn to a method and yet none of them recite sufficient elements to provide the claimed method. Claim 44, for example, includes the step of "providing reagents for use in an assay for binding" which still lacks any defining elements.

Claims 11 to 15, 19 to 22 and 44 to 50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are vague and indefinite because they recite the term "scavenger receptor protein type BI" as a limiting element and the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a scavenger receptor protein type BI. The fact that the claims recite additional elements does not avoid this rejection. A claim to "an isolated nucleic acid which hybridizes to a nucleic acid comprising the nucleic acid sequence of SEQ ID

NO:## under stringent hybridization conditions" is not vague and indefinite so long as stringent hybridization conditions are define in the specification. A claim which is drawn to "an isolated nucleic acid encoding a protein X and which hybridizes to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:## under stringent hybridization conditions" is vague and indefinite in the absence of a clear and concise definition of what is included and excluded by the term "protein X". The two elements "encoding a protein X" and "which hybridizes to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:## under stringent hybridization conditions" are two properties of a nucleic acid which are not mutually inclusive nor is one a subset of the other. The fact that a nucleic acid has either one of these properties does not mean that it will automatically have the other. Therefore, the fact that a claim recites the limitation "which hybridizes to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:## under stringent hybridization conditions" can not be relied upon as providing a definition for the term "a protein X".

Claims 11 to 12, 15, 19 to 22, and 44 to 50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are vague and indefinite because the term "hybridizing" is a conditional limitation and no conditions are recited in these claims.

Claim 14 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention. This claim is vague and indefinite in the recitation of the term "or a degenerate variant thereof". The term "degenerate" is recognized in the art of molecular biology as referring to a nucleic acid which encodes the same amino acid sequence as a reference nucleic acid but differs therefrom in nucleotide sequence. This is possible because the genetic code is "degenerate", which means that different codons can encode the same amino acid. Either the claimed nucleic acid encodes the amino acid sequence of SEQ ID NO:4 or it doesn't.

Claim 21 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is vague and indefinite because the physical relationship between the "molecule of claim 11" and the "expression vector" is critical to the claim but not recited therein. This claim should be directed to "an expression vector comprising the molecule of claim 11".

Claim 22 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is incorrect vague and indefinite because the physical relationship between the "composition of claim 21" and the "host cell" is critical to the claim but not recited therein. This claim should be directed to " a host cell comprising the...".

Claim 46 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention. This claim is confusing because the term "naturally occurring or synthetic compounds" implies that there is a third alternative.

Claims 11, 19 and 20 stand rejected under 35 U.S.C. § 102(a) as being clearly anticipated by the Calvo et al. publication (J. Biol. Chem. 268(25):18929-18935, 05 Sept. 1993) for those reasons of record in section 11 of Paper Number 7. Figures 2 and 3 on pages 18931 and 18932 of the Calvo et al. publication provided the nucleotide sequence of a recombinant DNA encoding a human protein that is identified therein as CLA-1 and the amino acid sequence of the protein encoded thereby. A comparison of the amino acid sequence of this protein with SEQ ID NO:4 of the instant specification clearly shows that CLA-1 is the human homolog of the hamster type BI scavenger receptor protein of the instant invention. The amino acid sequence of CLA-1 is identical to SEQ ID NO: 4, both of which are 509 amino acids in length, in 414 residues out of those 509 residues. Additionally, these sequences contain 62 conservative amino acid residue substitutions. Only 33 of the 509 residues in these two sequences do not match. These proteins are clearly species homologs of the same protein and both are encompassed by the term "scavenger receptor protein type BI" as defined in the instant specification. The labeled nucleic acid of claim 20 can be found in Figure 5 on page 18933 of this reference.

Appellant has attempted to antedate the Calvo et al. publication by demonstrating possession of an isolated DNA encoding a hamster scavenger receptor protein (SEQ ID NO:4) before the publication date of Calvo et al. Whereas this declaration is sufficient to avoid this

reference as applied to those claims which are limited to an isolated DNA encoding the amino acid sequence of SEQ ID NO:4 it does not show that Appellant was in possession of an isolated DNA encoding a human protein as described by Calvo et al.

This rejection is being withdrawn as applied to claim 12. Claim 12 was originally interpreted as reciting those cell types in which SR-BI/CLA-1 protein was naturally expressed, however, it is apparent from Appellant's arguments that the cells recited in claim 12 are intended to be recombinant cells which contain a heterologous nucleic acid encoding a SR-BI/CLA-1 protein. Such cells were not disclosed or suggested by Calvo et al.

Claims 21 and 22 are rejected under 35 U.S.C. § 103 as being unpatentable over the Calvo et al. publication (J. Biol. Chem. 268(25):18929-18935, 05 Sept. 1993) for those reasons of record in section 12 of Paper Number 7. These claims differ from those above in requiring the inclusion of the cDNA of Calvo et al. In an expression vector and host cell. As stated therein, the text in the seventh and eighth full paragraphs on page 18930 of the Calvo et al. publication shows that the expression of a recombinant DNA like that which was described in Figures 2 and 3 of Calvo et al. to obtain the isolated protein encoded thereby in quantity and to permit the characterization of that protein at the molecular level was routine in the art at the time of the instant invention. An artisan of ordinary skill, therefore, would have found it

*prima facie* obvious to have produced the CLA-1 protein of Calvo et al. by incorporating the cDNA described therein into an expression vector and heterologous host by employing those methods which were routine in the art at the time that the instant invention was made to permit the quantitative production of CLA-1 and to facilitate its characterization at the molecular level.

Claims 13 and 14 were inadvertently included in this rejection when it was restated in section 9 of Paper Number 10. However, as stated therein, "Applicant has antedated the Calvo et al. publication in so far as it is applicable to an isolated nucleic acid encoding a hamster CLA-1 protein by showing the isolation of a cDNA encoding hamster CLA-1 (a.k.a. BI) prior to the publication of the Calvo et al. publication". Since claim 14 is limited to an isolated nucleic acid encoding the amino acid sequence presented in SEQ ID NO:4 of the instant application, which is the hamster protein relied upon in the declaration to antedate the Calvo et al. publication, it is clear from the record that this rejection was no longer applicable to claim 14.

***(11) Response to Argument***

Claim 19 has been rejected under 35 U.S.C. 112, first paragraph, because it is specifically drawn to an isolated nucleic acid encoding a human scavenger receptor protein. No such nucleic acid is described in the instant specification in such detail as to show that Appellant was in possession of such a nucleic acid at the time that the instant application was filed. Appelant's arguments regarding enablement are misplaced since the instant rejection is

based upon a lack of adequate written description. Appelant's arguments in traversal of this rejection are in complete conflict with the recent decision cited above in *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), which has been relied upon in support of this rejection.

Claims 11 to 13, 17, 19 to 22 and 44 to 50 have been rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is not enabling for the production and use of an isolated nucleic acid encoding a scavenger receptor protein lacking one of the amino acid sequences that are disclosed in SEQ ID NOs:4, 6 and 8 of the instant application. Appellant notes that SEQ ID NO:6 is not a scavenger receptor protein. However, the instant specification meets all of the requirements of 35 U.S.C. 112, first paragraph, with respect to an isolated nucleic acid encoding a protein having the amino acid sequence presented in SEQ NO:6 of the instant application. With regard to the limitation of the claim to a nucleic acid encoding a "scavenger receptor protein type BI", section 8.1 of Paper Number 10 explains why this limitation is vague and indefinite and, therefore, it is not clear that a protein having the amino acid sequence of SEQ ID NO:6 would excluded by this limitation.

Applicant urges that the instant rejection is not applicable to claim 15 because it is limited to a nucleic acid having the exact amino acid sequence of SEQ ID NO:4. This rejection has been reconsidered as applied to claim 15 and withdrawn. Further. Appellant's arguments regarding the limitations of claim 14 are immaterial to the instant rejection since it has not been applied against claim 14.

Appellant apparently urges that the instant rejection of claims 11 to 13, 17, 19 to 22 and 44 to 50 under 35 U.S.C. 112, first paragraph, is inconsistent with the standards set forth in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). A *prima facie* case of non-enablement for the breadth of the claims was clearly articulated in the initial rejection and Appellant has not identified any error in the original factual basis upon which the rejection was made. Appellant is arguing that the single example presented in the instant specification of the isolation of a cDNA encoding a mouse protein by probing a mouse cDNA library with a cDNA encoding a hamster protein is a sound basis for claims which encompass any isolated nucleic acid which encodes any protein "which selectively binds to low density lipoprotein and to modified lipoprotein having the characteristics of acetylated low density lipoprotein".

Appellant has taken the position that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of

the artisan and the guidance presented in the instant specification and the prior art of record. Applicant's 'make and test' position is inconsistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), which were cited as the judicial basis for the instant rejection in the previous office action, and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). *In re Wands* stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of this factors were addressed in the initial rejection. The text beginning on line 38 on page 38 of the instant application indicates that "the "SR-BI" refers to the nucleotide and amino acid sequences, respectively, shown in shown in Sequence ID Nos. 3 and 4, and 7 and 8, and degenerate variants thereof and their equivalents in other species of origin, especially human, as well as functionally equivalent variants, having additions, deletions and substitutions of either nucleotides or amino acids which do not significantly alter the functional activity of the protein as a receptor characterized by the binding activity identified above". Because any nucleic acid will "hybridize" to any other nucleic acid under some conditions, the current claims encompass isolated nucleic acids encoding non-naturally occurring proteins having an amino acid sequence which completely deviates from the two naturally occurring amino acid

sequences disclosed in the instant specification. These claims encompass an unlimited number material embodiments. Breadth alone is not the issue, however. As stated on page 7 of Paper Number 7, *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Having established the breadth of the claims, *Wands* now requires that one consider the number of working examples presented in the instant specification. It is noted that there in not a single example in the instant specification, working or prophetic, of a scavenger receptor protein whose amino acid sequence deviates from nature. Since there are **no** working examples, then one must consider the guidance provided by the instant specification and the prior art of record. The instant specification provides absolutely no guidance as to which of the amino acid residues in either of SEQ ID Nos:4 and 8 of the instant application are essential for the functional and structural integrity of a scavenger receptor protein and which residues are either substitutable or expendable. Further, there is no functionally and structurally

analogous protein which has been identified in the prior art for which this information is known and could be extrapolated to a scavenger receptor protein by analogy. In conclusion, the instant claim encompasses isolated nucleic acids encoding a vast, almost limitless, number of scavenger receptor proteins having non-naturally occurring amino acid sequences and yet the instant specification provides no working examples and no guidance that would permit and artisan to practice the invention commensurate with the scope of the instant claims.

Applicant's argument is based upon a premise that the standard under 35 U.S.C. ¶ 112, first paragraph, is that of mutating a subject protein and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts, as shown by those decisions cited above.

Further, *In re Wands* determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally occurring compounds and the instant specification does not provide a description of a repeatable process of producing an isolated nucleic acid encoding a scavenger receptor protein whose amino acid deviates from either of the two disclosed, naturally occurring rodent sequences. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner

which would involve the determination of those amino acid residues in the amino acid sequence of either of SEQ ID Nos:4 and 8 which are required for the functional and structural integrity of that protein. It is this additional characterization of those two disclosed, naturally occurring, rodent proteins that is required in order to obtain the functional and structural data needed to permit one to produce an isolated nucleic acid encoding a scavenger receptor protein which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

Appellant relies upon a board decision in *Ex parte Mark*, 12 USPQ2d, 1904 (Bd. Pat. App. and Int., 1989) to support an argument that 'mutate and test' is the standard under 35 U.S.C. § 112, first paragraph. On the contrary, the modification of any protein by the substitution of a different amino acid residue for a nonessential cysteine residue was enabled by that specification since the art of protein chemistry, in light of the working examples and guidance provided by that specification, was believed to be sufficiently predictable that this change could be made in any protein with a reasonable expectation that the modified protein would retain its original function and that the disclosed advantages of making this modification would be realized. The inventive contribution of Mark et al. was not a particular protein product but a specific modification which could be made to any protein with a reasonable amount of predictability and which would achieve a disclosed and specific advantageous result. This decision, therefore, does not support Applicant's position and it is in conflict with the instant rejection.

With regard to the propriety of specifically considering the decisions of *In re Fisher*, *Amgen Inc. v. Chugai*, and *In re Wands* to the exclusion of the plurality of decisions cited by Applicant in determining the patentability of the instant claims, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph in a recent CAFC decision, *Genentech, Inc. v. Novo Nordisk*, 42 USPQ2d, 100 (CAFC 1997), in which these three decisions were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a **reasonable expectation** that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are **more likely to work that not** without actually making and testing them then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that any nucleic acid which hybridizes to one of the two disclosed nucleic acids under non-specific conditions will encode a protein which will more likely than not perform in the manner disclosed and the instant specification.

Applicant has traversed the rejection of claims 11, 19 and 20 under 35 U.S.C. § 102(a) as being clearly anticipated by the Calvo et al. publication (J. Biol. Chem. 268(25):18929-18935, 05 Sept. 1993) on the premise that the isolation of a single DNA encoding a hamster scavenger receptor protein in conjunction with the knowledge that it was structurally related to "Rat LimpII" and CD36, as described in the declaration by Monty Krieger and Susan L. Acton, which was filed on 05 January of 1998 under 37 C.F.R. § 1.131, shows a reduction to practice of a genus of DNAs which includes the cDNA that was described in Figures 2 and 3 of the Calvo et al. publication as encoding a human protein identified therein as CLA-1. Appellant contends that they were in possession of information regarding SR-BI/CLA-1 protein from animals other that hamster and attempt to support this assertion by showing that Appellant was aware that the most closely related proteins to hamster SR-BI/CLA-1 protein (a.k.a. class B1 scavenger receptor protein, a.k.a. SR-BI) which could be found by sequence search were "Rat LimpII" and human CD36. Contrary to Appellant's assertion, "Rat LimpII" and CD36 are not "CLA-1" proteins. As Appellant has expressly stated on page 48 of their brief "CD36 and SR-BI are *not* the same proteins nor do they have the same binding activity". It is a fact that the declaration provided by Appellant has not demonstrated the possession of any isolated nucleic acid or protein **not known in the prior art** other than the hamster protein identified in the instant specification as "hamster class B1 scavenger receptor protein".

Appellant has been advised that the declaration provides no evidence that the nucleic acid described therein was capable of hybridizing to mouse DNA. Appellant urges that this statement is in error by pointing out that **the instant specification** describes mouse DNA encoding an SR-BI (CLA-1) protein. Appellant urges that "the specification provides exactly the type of evidence the Examiner is looking for". Appellant can not rely upon the content of the specification to antedate a reference. As stated earlier, there is no evidence **in the declaration** by Monty Krieger and Susan L. Acton that the hamster cDNA described therein would selectively hybridize to a nucleic acid encoding a homologous protein from any other animal and there was no evidence that the proteins CD-36 and LIMP II were known to be conserved between species since only a single orthologue of each of these proteins was described in the declaration. In fact, it is Figure 1 of the Calvo et al, publication which first demonstrates that LIMP II is conserved between rodents and humans. *In re Clarke*, 148 USPQ 665, (CCPA 1966) held that;

> " It appears to be well settled that a single species can rarely, if ever, afford support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.21 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of a small genus such as halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the

case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary."

The declaration shows that Appellant was in possession of only one species of the now claimed genus of isolated nucleic acids at the time of the Calvo et al. publication and this single species of nucleic acid, which encoded a hamster SR-BI/CLA-1 protein, did not anticipate or render obvious the isolated cDNA encoding the human SR-BI/CLA-1 protein that was described by Calvo et al.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

JOHN ULM
PRIMARY EXAMINER
GROUP 1800

JDU
May 14, 1999

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600